PATENT
Customer No. 22,852
Attorney Docket No. **02481.1693**

IN THE UNITED STATES PATENT AND TRADEMARK OFFICE

In re Application of:	)	
	)	
HABERMANN et al.	)	Group Art Unit: 1656
	)	
Application No.: 09/664,326	)	Examiner: Holly G. Schnizer
	)	
Filed: September 18, 2000	)	Confirmation No.: 4393
	)	
For: **SIGNAL SEQUENCES FOR PREPARING LEU-HIRUDIN BY SECRETION BY E. COLI INTO THE CULTURE MEDIUM**	)	

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Commissioner for Patents
P.O. Box 1450
Alexandria, VA 22313-1450

Sir:

PRE-APPEAL BRIEF REQUEST FOR REVIEW

In accordance with the provisions in the Patent and Trademark Office Official Gazette Notice entitled "New Pre-Appeal Brief Conference Pilot Program" of July 12, 2005, Applicants respectfully request a pre-appeal brief review of the rejections in the Final Office Action dated May 30, 2006 (Office Action). This Request is being filed concurrently with a Notice of Appeal, before the filing of an Appeal Brief, and complies with the requirements set forth in the aforementioned Official Gazette.

REMARKS

I. Status of the claims

Claims 6-9 have been at least twice rejected and are the only pending claims in this application. No claim is being amended in this Request.

II. Claim rejections under 35 U.S.C. § 112, first paragraph

The Office rejected claims 6-9 under 35 U.S.C. § 112, first paragraph, as failing to comply with the written description requirement. The Office argues that "[t]he added limitation that the E. coli bacteria used in the process are not E. coli secretor mutants is considered new matter."

The amendment claiming a process "wherein the E. coli bacteria are not E. coli secretor mutants" finds proper support in the specification

The Office argues that although "the specification mentions E. coli strain Mc1061, [an E. coli non secretor mutant,] the specification does not indicate which E. coli strain (Mc1061 or WCM100) was used in the disclosed tests and which gave the expression that was 1.5 times better than the comparative test." Office Action at paragraph bridging p. 2-3.

Respectfully, the Office has not applied the proper standard to determine whether Applicants' amendment complies with the written description requirement of 35 U.S.C. § 112, first paragraph. The standard is "whether the specification conveys with reasonable clarity to those skilled in the art that, as of the filing date sought, [applicant] was in possession of the invention [as] now claimed," *i.e.*, whether Applicants were in possession of the claimed method wherein the *E. coli* bacteria are not *E. coli* secretor mutants. M.P.E.P. § 2163.02.

The passage in question reads:

> Competent cells of the E. coli strain Mc1061, or the secretor mutant WCM100, were transformed with the ligation mixture and grown under selection pressure on ampicillin-containing plates. The next morning, expression as described in Example 6 was then compared with the Ala-hirudin expression using *E. coli* strain WCM100/pCM7053. It was found that the expression obtained was about 1.5 times better than in the comparative test. Specification at p. 9, lines 1-6 (underlining added).

The underlined portion of the passage clearly indicates that Applicants were in possession of methods wherein *both E. coli* strain Mc1061 (a non secretor mutant) *and* the secretor mutant WCM100 were used. Upon reading the underlined section, one of ordinary skill in the art would understand that Applicants contemplated using *E. coli* strain Mc1061 and secretor mutants in the methods of the invention, and, therefore, were in possession of such methods. The Office's concern regarding which *E. coli* strain (Mc1061 or WCM100) gave the expression that was 1.5 times better than the comparative test is immaterial to whether Applicants were in possession of the claimed methods. Regardless of which strain gave the improved expression, Applicants already have demonstrated that they were in possession of a method using either strain.

A genus of E. coli bacteria that are not E. coli secretor mutants is fully supported by the specification

The Office further argues that "while the specification may provide support for using the E. coli strain Mc1061 in the claimed method, it does not support using a genus of E. coli strains that are not secretor mutants." *Id.* at p. 3.

The disclosure in the working examples of *E. coli* strain Mc1061 is not the only disclosure of non secretor mutants. As examples, Applicants cite the following passages:

> An object of the present invention is accordingly to prepare a fusion protein, wherein the combination of signal sequence and Leu-hirudin

> permits direct processing to Leu-hirudin and subsequent secretion of native Leu-hirudin in high yields by *E. coli*. Page 2, lines 19-21.
>
> Another aspect of the invention is a process for preparing Leu-hirudin, in which...(b) the expression plasmid from (a) is expressed in a suitable *E. coli* cell. Page 5, lines 11-15.
>
> A further aspect of the invention is a process for finding a suitable signal peptide for secretory expression of any desired protein in *E. coli*. Page 5, lines 21-22.

These passages clearly convey to one of ordinary skill in the art that Applicants were in possession of methods wherein *E. coli* bacteria in general were used, regardless of whether the *E. coli* bacteria are or not secretor mutants. The Office has already admitted that "the specification as a whole teaches that any E. coli strain could be used" in the methods of the invention. Office Action at bottom of p. 4. Having described experiments were secretor mutants were used (*see, e.g.*, the working Examples) Applicants are now carving out subject matter drawn to those secretor mutants from the claims. The propriety of this claim amendment is supported by the M.P.E.P. and case law. For example, it has been recognized that inventors may claim less than the full scope of their disclosure and that "[i]f alternative elements are positively recited in the specification, they may be explicitly excluded in the claims." M.P.E.P. § 2173.05(i) (citing *In re Johnson*, 558 F.2d 1008,1019 194 U.S.P.Q. 187, 196 (C.C.P.A. 1977)).

Finally, Applicants have the statutory right to select, from what is disclosed in the specification, the subject matter they regard as their invention. U.S.C. 35 § 112, ¶ 2. And, the courts have specifically recognized that "[s]ince the patent law provides for the amendment during prosecution of claims, ...the second paragraph of 35 U.S.C. § 112 does not prohibit the applicant from changing what he 'regards as his invention' (i.e. the

subject matter on which he seeks patent protection) during the pendency of his application." *In re Saunders*, 444 F.2d 599, 607, 170 U.S.P.Q. 213, 220 (C.C.P.A. 1973).

III. Conclusions

In view of the foregoing remarks, Applicants respectfully request reconsideration of the rejections in the Final Office Action and the timely allowance of the pending claims.

Please grant any extensions of time required to enter this response and charge any additional required fees to our deposit account 06-0916.

Respectfully submitted,

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